Conclusions

With the STS, TPI, and RPCF tests, the detection of three distinct antibodies is possible in syphilis. It is suggested that the ideal combination of tests for the diagnosis of the treponematoses is the RPCF test and two tests for reagin, one of standard and one of high sensitivity, with the TPI test as a confirmatory test.

In the combination of a reagin test and the RPCF test, the occurrence of a positive reaction in both should have a specificity of over 99·99 per cent., that is one false positive in over 10,000 patients, and a sensitivity for bacteriological syphilis considerably higher than that of the STS of acceptable specificity. Discrepant results should be checked with the TPI test, which remains the final standard and is the only test of suitable specificity to distinguish between biologic false positive reactions and certain cases of syphilis. This test system would provide the clinician with an immediate, reliable serologic diagnosis in most of the cases which now cause difficulty; those patients in whom there was delay would comprise the biologic false positive reactors, some with treated syphilis, and a small proportion with active infections.

Summary

The treponemal Wassermann reaction (TWR) and the Reiter protein complement-fixation test (RPCF test) were examined and their results compared with the clinical findings and the TPI test. The TWR was found to be of an unsatisfactory degree of specificity for use as a routine or confirmatory test. The specificity and sensitivity of the RPCF test were found to be higher than those of the STS.

It is suggested that the ideal combination of tests for the diagnosis of the treponematoses is the RPCF test and two tests for reagin, one of normal and one of high sensitivity, and that discrepancies between the reagin tests and the RPCF test should be submitted to the TPI test.

Thanks are due to the Board of Governors of the Royal Free Hospital for facilities to carry out this work, and especially to my technicians, Mr. A. E. Eldridge and Mrs. Doreen Birch for their unstinted help, and also to the many clinicians and pathologists who have contributed the material used in this study.

REFERENCES

Bordet, J., and Gengou, O. (1901). *Ann. Inst. Pasteur*, **15**, 289.
Browning, C. H., Cruickshank, J., and M'Kenzie, I. (1910). *J. Path. Bact.*, **14**, 484.
D'Allessandro, G., and Oddo, F. (1948). *Riv. Ist. sieroter. ital.*, **23**, 119.
——, ——, and Dardanoni, L. (1950). *J. vener. Dis. Inform.*, **31**, 314.
Detre, L. (1906). *Wien. klin. Wschr.*, **19**, 619.
De Bruijn, J. G., and Bekker, J. H. (1957). *Ned. T. Geneesk.*, **101**, 1615.
Foster, W. D., Nicol, C. S., and Stone, A. H. (1958). *Brit. J. vener. Dis.*, **34**, 196.
Gaehtgens, W. (1929). *Z. Immun.-Forsch.* (Orig.), **63**, 398.
——(1937). *Arch. Derm. Syph.* (*Berl.*), **176**, 42.
Hardy, P. H., and Nell, E. E. (1955). *J. exp. Med.*, **101**, 367.
—— ——(1957). *Amer. J. Hyg.*, **66**, 160.
Landsteiner, K., Müller, R., and Poetzl, O. (1907). *Wien. klin. Wschr.*, **20**. 514.
Magnuson, H. J., and Portnoy, J. (1956). *Amer. J. Publ. Hlth*, **46**,190.
Marie, A., and Levaditi, C. (1907). *Ann. Inst. Pasteur*, **21**, 138.
Nelson, R. A. (1953). *Science*, **118**, 733.
—— and Diesendruck, J. A. (1951). *J. Immunol.*, **66**, 667.
—— and Mayer, M. M. (1949). *J. exp. Med.*, **89**, 369.
Nichols, H. J., and Hough, W. H. (1913). *J. Amer. med. Ass.*, **60**, 108.
Portnoy, J., and Magnuson, H. J. (1955). *J. Immunol.*, **75**, 348.
Price, I. N. Orpwood (1948). *J. clin. Path.*, **1**, 91.
——(1950). *Brit. J. vener. Dis.*, **26**, 172.
——(1958). *Ibid.*, **34**, 91.
—— and Whelan, M. J. (1957). *Ibid.*, **33**, 18.
—— and Wilkinson, A. E. (1952). *Ibid.*, **28**, 16.
Puccinelli (1952). *Ibid*, **28**, 184.
Rein, C. R., Kelcec, M. T., D'Alessandro, G., and De Bruijn, J. G. (1957). *J. invest. Derm.*, **28**, 459.
Ruge, H. G. S. (1956). *Brit. J. vener. Dis.*, **32**, 242.
Sachs, H. (1911). *Berl. klin. Wschr.*, **48**, 2066.
Turner, T. B. and Hollander, D. H. (1957). "Biology of the Treponematoses". WHO Monograph Series No. 35. W.H.O., Geneva.
Wassermann, A. von, and Ficker, M. (1922). *Klin. Wschr.*, **1**, 1101.
——, Neisser, A., and Vruck, C. (1906). *Dtsch. med. Wschr.*, **32**, 745.
Wilkinson, A. E. (1957). *Brit. J. vener. Dis.*, **33**, 25.
Witebsky, E. (1929). *Z. Immun.-Forsch.*, **62**, 35.

DISCUSSION

The President, DR. R. M. WARREN (*Southampton*) thanked the speakers for their excellent papers. Anything leading to the more accurate diagnosis of disease would be universally welcomed and, for this reason, these contributions were particularly timely.

The point that occurred to him was that the persistence of a positive reaction to the RPCF test after treatment might lead to difficulties in assessing the adequacy of treatment.

DR. T. E. OSMOND (*London*) asked for how long the RPCF test would remain positive after the adequate treatment of primary, secondary, and late syphilis?

DR. SEQUEIRA said he could not answer this question as the time for sero-reversal appeared to vary very much from case to case and was not related to that of the reagin tests.

DR. W. V. MACFARLANE (*Newcastle-on-Tyne*)

asked whether the RPCF test had reached the stage at which the routine STS could be dispensed with.

DR. SEQUEIRA answered that he regarded the routine and treponemal tests as complementary and that the routine STS should not be dropped, as testing would again depend on one antibody, with which there was less experience than with reagin.

MR. A. J. KING (*Whitechapel Clinic*) stated that what had been hoped for from the TWR and RPCF test was an inexpensive substitute for the TPI test. On the present evidence he could not see that either was likely to supply this need. It seemed clear that the RPCF test was valuable, to an extent which was not yet fully assessed, but the final court of appeal in cases of serological difficulty remained the TPI test.

DR. A. E. WILKINSON (*V.D. Reference Laboratory*) said that he had been interested in the Reiter spirochaete for a long time. The strain of spirochaetes that he was using at that time appeared to differ materially from the illustration of the original Reiter spirochaete shown by Dr. Sequeira. It might be that the organism itself had changed over the years. He had first used killed spirochaetes as an antigen and had obtained results more specific and sensitive than those obtained with the standard tests. A year ago he had started using the protein antigen and his results were in broad agreement with those of Dr. Sequeira. Taking blood donors, in whom standard tests were negative, no positive result had been obtained in 149 tested with the RPCF test. Of 133 cases of chronic syphilis (both treated and untreated) tested with the TPI test, 118 were found to be positive, whereas the RPCF test was positive in 98, the TWR in 89, and the standard tests in fewer still. In cases of proven syphilis, Reiter's test appeared to be more sensitive than the standard tests. In "problem" sera, there had been a very close agreement between the RPCF and TPI tests. Of nearly 800 sera, 254 were found positive to the RPCF and all but six of these had positive TPI tests. In RPCF negative cases, the agreement was not quite so close; in 534 RPCF-negative sera the TPI was positive in nearly 17 per cent. Probably this was because he had not used overnight incubation.

In general, his figures agreed with those described during the evening and with those reported earlier from the U.S.A. The RPCF was a simple and inexpensive test which formed a most useful addition to the battery of tests. The next stage in the evaluation of this test should consist of serial tests on known treated syphilitic patients so that the behaviour of the test could be outlined. This had not yet been done and it was important that the experiment should be carried out.

DR. C. S. NICOL (*St. Thomas's Hospital, London*) fully agreed that the RPCF test could not replace the routine serological tests for syphilis, but he thought the new method could provide useful information as a screening test. STS-negative and RPCF-positive sera could then be submitted for TPI testing. If the TPI was positive, the diagnosis of treponemal disease was confirmed. If the TPI was negative, further full investigation was still needed. A careful clinical assessment of patients in the St. Thomas's series had been carried out. He considered that RPCF-positive, TPI-negative patients who had suffered from gonorrhoea in the past could also have had the opportunity of acquiring syphilis.

Many patients had received penicillin and other antibiotics for various reasons before being seen at the clinic; routine RPCF testing suggested that the incidence of syphilis had not fallen as much as had been thought. The problem was which patients with positive RPCF tests required treatment. They should certainly all be investigated.

Referring to the president's opening remarks, he agreed that a persistently positive RPCF test did not indicate treatment failure, and that this point required further investigation.

The technique of the RPCF test as performed at St. Thomas's was simple and he had found that the information obtained was a valuable help in clinical work.

DR. WARREN asked whether the RPCF test could be recommended to local laboratories for performance in parallel with the STS.

DR. SEQUEIRA replied that it would be premature to use the test in this way.

DR. J. A. H. HANCOCK (*Whitechapel Clinic*) stated that Dr. Wilkinson had raised the point that the next step was the investigation of the RPCF in known cases of syphilis. He had started such an investigation elsewhere, and he described two cases of tabes with negative standard tests and RPCF, but positive TPI tests.

DR. E. M. C. DUNLOP (*Whitechapel Clinic*) asked Dr. Sequeira what proportion of the patients tested by means of the TWR were coloured. In making a clinical assessment of the TWR he had found a high proportion of positive findings in coloured patients. He thought it could be misleading to regard a single TPI as the absolute and final court of appeal in cases of serological difficulty. Like all serological tests the TPI appeared open to error, and in cases where two tests had been performed he had found several in which they disagreed.

DR. SEQUEIRA stated that, in general, the reproducibility of the TPI test was as high as that of most accepted tests.